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Electrostrictive energy in cancer cells – Modelling based on Nyquist Criterion

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Abstract

Electrostrictive Energy (ESE) in human cells is a useful diagnostic tool in detection of cancer if it can be measured cost effectively. This paper derives this energy mathematically from results of experimentally verified Capacitance Relaxation (CR) phenomenon of human cells (US patent 5691178, 1997) and establishes the correlation between CR phenomenon and ES energy in cancer cells using Nyquist criterion. The approach is based on the behavior of human cells formed of a bi-layer of highly mobile lipid molecules. The human cells exhibit different dynamic capacitances and associated electrostrictive energy when they are normal and when affected by cancer. Normal cells behave like a dielectric while cancer cells exhibit the characteristics of a composite leaky dielectric. The paper establishes, through modeling, that normal cells behave like first order control systems while cancer cells behave like higher order systems accounting for different ES energy in both cases. This corresponds to the established theory that during the process of DNA synthesis and cell division, changes in the membrane capacitance for the first order system is relatively slower compared to that in cancer cells. This also correlates with the situation where the membrane potential falls during cell division and DNA synthesis in normal cells, the difference being that cell division here leads to carcinogenic changes. .

Keywords : Capacitance Relaxation phenomenon, ES energy, dielectric (pure, leaky and composite leaky)

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1. Introduction

1.1 . Electrostriction [6], [1], [8] is a property of all dielectric materials and is caused by the presence of randomly-aligned electrical domains within the material. It is generally defined as the deformation of a dielectric body as the result of an applied electric field. When an electric field is applied to the dielectric (say by trans-membrane potential of around 100 mv), the opposite sides of the domains become differently charged and attract each other, reducing material thickness in the direction of the applied field (and increasing thickness in the orthogonal directions due to Poisson's ratio). More formally, the electrostriction coefficient is a fourth rank tensor, relating to second order strain and first order polarization tensors [1]. First order compression related to polarization is reversible while the second order strain due to electrostriction is irreversible. Since the process of second order strain is irreversible (reversal of electric field does not reverse direction of dformity), elastic energy is stored in the dielectric as long as the applied field is present. This energy is the electrostrictive energy [8].

2. Characteristics of cells – normal and malignant [8]

2.1. Normal human cells (healthy cells) behave like a dielectric (insulator that prevents movements of charged ions across the membranes except through special passages) and have certain capacitance value. Major charged ions mentioned above comprise negatively charged electrons and anions (particularly phosphate ions) and positively charged hydrogen protons, sodium, potassium,

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calcium and magnesium ions. As the cell membrane is selectively permeable to sodium and potassium ions, there is a different concentration of ions on either side of the membrane and this causes the trans-membrane potential of -60 to -100 mv, the - sign indicating a higher negative charge inside the cell

2.2. Any condition like illness (for example cancer) alters the cell membrane and its permeability and thus the sterol and lipid content of the cell itself. The altered membrane permeability results in the movement of potassium, magnesium and calcium (all –ve charge) out of the cell and injestion of water soluble sodium (+ve charge) and water into the cell. Thus cancer cells act like a composite leaky dielectric. As a result of these mineral movements in and out of the cell, membrane composition changes leading to energy abnormalities and charge distribution abnormalities. These abnormalities result in a fall in trans-membrane potential and rise in membrane capacitance (Capacitane Relaxation at around 200 Hz of applied potential) [2], [3], [4]. The excessive amount of negative charge on the exterior surface of the cell (as a result of mineral movement) lead to cellular electrical abnormalities and bring about carcinogenic and genetic changes [5]. Two distinguishing electrical features of cancer cells are 1. They maintain their membrane potential at lower value (compared to -60 to -100 mv in normal cells) and 2. The intracellular sodium concentration is of a higher value (due to leaky dielectric and ingestion of sodium into cell) [2]. Sustained elevation of intracellular sodium may act as a mitotic trigger leading to mitosis and cell division. During the process of normal cell division and DNA synthesis, the membrane potential falls to around -15 mv. Fall in membrane potential of cancer cells due to altered permeability of membrane has similar membrane potentials and hence the mitotic trigger.

Relaxation of normal (healthy) cells and malignant cells are shown in Figs 1(a) and 1 (b) [7]. These graphs were outputs of models of the type $1/(s + a)$ (First order – Fig 1 (a) for normal cells) and $1/(s^2+s+1)$ (Second order for cancer cells – Fig 1 (b)) respectively in MATLAB simulation (coefficients of s terms were found by trial and error). Simulated output of the model of type $1/s^2+s+1$ is shown in Fig 1 (c) corresponding to actual curve in fig 1(b). Cancer cells demonstrate higher conductivity and permittivity compared to normal cells and they cover a larger surface area. This property is reflected in the jump in capacitance established by the Capacitance relaxation phenomenon (A to B in Fig. 1(c)). Accordingly, the cancer cells can be modelled as second order systems having a transfer function of the type $1/(s^2 + s + 1)$

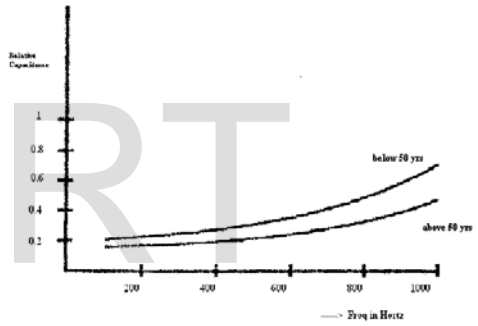

Fig 1(a)

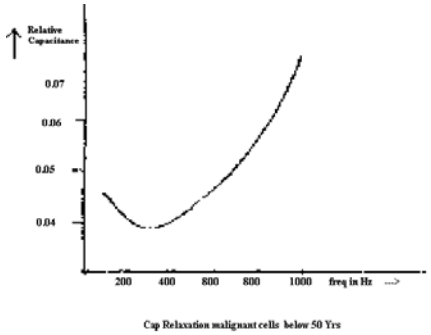

Fig 1(b)

3. Modelling

3.1 Experimental results of Capacitance

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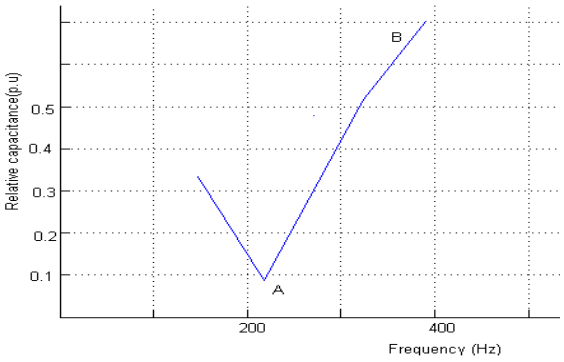

Fig 1(c)

3.2 Mathematical derivation of ES energy from CR results. In order to calculate the electrostrictive energy in cancer cells, the following approach was employed by the research scholar [8] :

(a) With incremental changes in capacitance (when it starts to relax - Region A to B in Fig 1 (c)) as input to this second order system model, the output is focused to trace out the locus from which it is possible to obtain electrostatic surfaces containing negative charges. This is done for different increments of capacitance change in the forward (A to B) and for same decrements in reverse (B to A) paths in Fig 1(c). See Fig 2. Nyquist criterion in MATLAB has been used to trace out the loci from A to B and then, B to A [8].

(b) The difference in electrostatic surface areas of forward and reverse paths for a given increment in capacitance value (Fig 2 (a) – Fig 2 (b) = Fig 2 (c)) gives the variation in electrostrictive energy ($\Delta\varepsilon S$) for that increment.

(c) This exercise can be carried out for different capacitance increments starting from A and going towards B and then in the reverse path of B to A in Fig 1(c) for simulated capacitance relaxation curves of both normal and malignant cells.

3..2.1 **An example derivation.** One example of such calculation is shown for cancer cells exhibiting properties of a second order system of the type $1/(s^2 + s + 1)$ in Figs 2(a), 2(b) and 2(c). The example is for $\Delta C1$ (capacitance change from 0.4 to 0.5 p.u in Fig 1(c) which is the CR output for the second order malignant cells). The electrostatic surfaces obtained for to forward (A towards B in Fig 1(c)) and reverse path (B towards A in Fig 1(c)) for this $\Delta C1$ are given in Figs. 2a and 2b. The difference in electrostatic surface areas of Figs 2a and 2b (as shown in Fig 2c) gives the change in electrostrictive energy ($\Delta\varepsilon S$) which is 0.15 p.u in this case. Similar values of $\Delta\varepsilon S$ for $\Delta C2$ (0.3 – 0.4), $\Delta C3$(0.2 – 0.3) and $\Delta C4$(0.1 – 0.2) are shown in Fig 3 for these increments in ΔC as 0.12, 0.06, and 0.03 p.u for $\Delta C2$, $\Delta C3$ and $\Delta C4$ respectively) and tabulated in Table 1 for malignant cells.

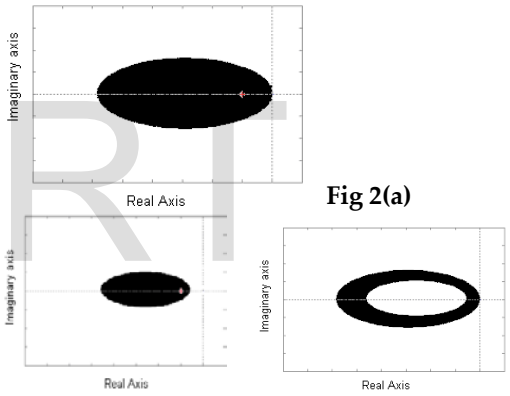

Fig 2(a)

Figs 2 (b) **Fig 2(c)**

Fig 2 Electrostatic Surface area for $\Delta C1$ (a) Fwd path (b) Rev path (c) Diffce in area

3.2.2. The variation of electrostrictive energy as a function of incremental changes in capacitance of malignant cells, calculated as above, is shown in Fig 3 for a second order system (malignant cells). For incremental changes in capacitance of the cells (from Fig 1(c)), the electrostrictive energy in the cell decreases progressively (exponentially) in the case of cancer cells as the capacitance jumps due to relaxation as can be seen in Fig 3. It can be seen that, before A, capacitance change is more (first order) while in the region A to B, the capacitance value jumps but changes slowly (non linear system), thus establishing correlation between ES energy and capacitance relaxation.

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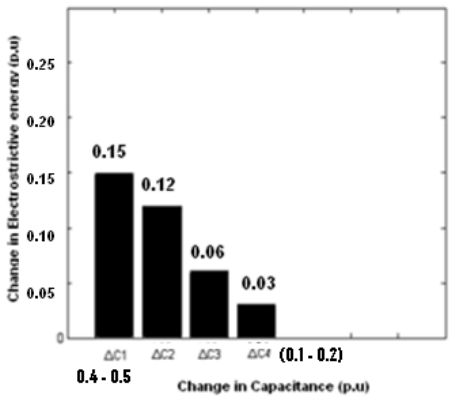

Fig 3 Per Unit Electrostrictive energy of cancer cells vs variations in cell capacitance

3.5 **Changes in ES Energy.** The changes in electrostrictive energy (ΔεS) for incremental changes in capacitance ΔC in Fig 3 for cancer cells follow a second order system model [8]. Thus, the electrostictive effect of cancer cells in conjunction with Capacitance Relaxation phenomenon is related to the membrane acting as a composite leaky dielectric material represented by a second order transfer function in simulation. In the model, the electrostrictive energy decreases with differential changes in capacitance of the cell membrane. While normal cell membranes behave like a first order system represented by higher electrostrictive energy and a slow process of cell division and DNA synthesis (close to region A), the electrostrictive energy for the same incremental changes in capacitance of cancer cells is lower (close to region B) compared to normal cells and the simulated model for cancer cell membranes behaves like a second order system. The simulation above using Nyquist

ΔC See Fig 1 (c)	Incremental relative capacitance changes In reverse path B to A, Fig 1 (c)	ΔεS Change in εS energy II Order system (Cancer Cells) Fig 3 & 1(b)	ΔεS Change in εS energy I Order system (Normal Cells) Fig 1 (a)
ΔC1	0.4 to 0.5	0.15	0.4
ΔC2	0.3 to 0.4	0.12	Higher than II order system
ΔC3	0.2 to 0.3	0.06	-----do -----
ΔC4	0.1 to 0.2	0.03	---- do ------

Table 1 Variation of ES Energy with CR in cancer cells

criterion can be carried out for a first order system (of type 1/s+1) representing normal cells. In this case, for ΔC1 of 0.4 to 0.5, the value of ΔεS = 0.4 while the corresponding value of ΔεS is 0.15 in a second order system as seen from Table [2], [8]. Thus, this simulation establishes the fact that the electrostrictive energy is less for cancerous cells compared to that of normal cells for similar incremental changes in capacitance and that the ES energy progressively decreases with differential changes in capacitance of malignant cells. It can be noted that during process of cell division and DNA synthesis in respect of a composite dielectric is relatively slow and hence is assumed to be of first order. But for the same incremental change in capacitance, change is ES energy is much higher (0.4) in a first order system than in a second order system (0.15). A similar exercise was carried out for simulated curve of Fig 1 (a) and Control system of type 1/(s + a) representing normal healthy cells. Table 1 lists the incremental capacitance changes for both normal and malignant cells.

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3.2.3 **Summary.** The following, thus, summarizes the effect of Capacitance relaxation and electrostriction phenomena in respect of normal and malignant cells :

(a) In normal cells, the membrane capacitance is low, the membrane is a good dielectric, membrane potential is high, electrostrictive energy stored is high and the whole cellular homeostasis system behaves like a first order system

(b) In the case of malignant cells, due to presence of more water and enlarged area, the membrane becomes a composite leaky dielectric with lower membrane potentials, higher capacitance and lower electrostrictive energy. In essence, the cellular homestasis system in this case behaves like an ordered system (II and higher orders).

(c) The electrostrictive energy for first order (normal cells) and second order (malignant cells) systems can be derived from Capacitance relaxation curve for normal and malignant cells using Nyquist creiterion as detailed in section 3.2.

(d) Electrostrictive energy stored in cells (normal and malignant) correlates directly with the experimentally verified capacitance Relaxation phenomena in normal and malignant cells and thus can be derived from the latter using Nuquist criterion as explained.

4. Disussion and conclusions

Electrostrictive energy stored in cancer cells has a direct correlation with experimentally verified Capacitance Relaxation phenomenon [7]. The energy in reduced quantum results from composite property of cell membrane that has become leaky and has altered permeability and is no longer a pure dielectric (insulator). Normal cells that exhibit capacitance characteristics as per Fig 1(a) behave like I order systems (of transfer function of the type 1/(s+a)) on simulation of curve at Fig 1(a). However, malignant cells with capacitance profile as shown in Fig 1(b) behave like ordered system (II and higher order) on simulation by MATLAB of the type $1/(s^2 + s + a)$. Higher order systems have lesser ES energy stored in the cells compared to normal healthy cells. Elevated levels of sodium in intracellular fluid bring about acidosis environment and can act as a mitotic trigger leading to (carcinogenic) cell division and growth. If the Electrostrictive enegy can be measured cost effectively (research is going on in this respect), it could be a good diognastic toll for detection of cancer.

References

[1] Blatt, FJ. 1982 'Elastic energy stored in a membrane due to electrostriction', *Journal of Biological Physics* , Vol 10 No 4

[2] Cone, CD. 1970, 'Variation of transmembrane potential level as a basic mechanism of mitosis control', *Oncology* 1970, 24 pp 438-470

[3] Cone CD 1975 The role of surface electrical transmembrane potential in normal and malignant mitogenesis, *Ann. NY Acad Sci. 1975, 238 pp 420-435*

[4] Cone CD 1985 Transmembrane potentials and characteristics of immune and tumour cellsBoca Raton Florida *CRC Press.*

[5] Cure JC 1991 Cancer, an Electrical phenomenon *Resonant* 1991.1.1

[6] Daniel VV Dielectric relaxation *Academic Press* London 1967

[6]. Daniel VV Dielectric Relaxation Academic Press London 1967

[7] Shaw P, Basak TK, Ghosh NC 2006 Capacitance Relaxation phenomenon in cartilaginous membrane *Every Man's Science* Vol XL No 6.

[8] Tapas Kumar Basak, Ramanujam T, Suman Halder, Poonam Goyal,PM Kulshreshta, Shweta Pandey, Himanshu Tripathi 2008 'Electrostrictive effect in cancer cells reflected in Capacitance Relaxation phenomenon' *Sesnors & Transducers vol 99 issue 12* Dec 2008 pp 90-101.

